IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

MERCK & CO., Inc. Plaintiff, v. RANBAXY INC. and RANBAXY LABORATORIES LIMITED, Defendant.	C.A. No. 07-229 (GMS)
RANBAXY INC. and RANBAXY LABORATORIES LIMITED, Counterclaim Plaintiff, v. MERCK & CO., Inc. Counterclaim Defendant.	

BRIEF ON CLAIM CONSTRUCTION OF DEFENDANTS
RANBAXY INC. AND RANBAXY LABORATORIES LIMITED

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Defendants Ranbaxy Inc. and Ranbaxy Laboratories Limited (collectively "Ranbaxy") submit the present brief in support of Ranbaxy's proposed claim construction.

I. INTRODUCTION

The claims of U.S. Patent 5,147,868 ("the '868 patent")[1] (A1-20)[2] are directed to various genera encompassing compounds within the scope of formulas set forth in Claims 1 and 9, and to methods of using these compounds to inhibit the activity of dipeptidase. (Claims 21 and 22). The compounds are said to selectively inhibit the metabolism of dipeptidase (E.C.3.4.13.11) ('868 1:20-44), but none of the compound claims at issue contains any limitation with respect to activity or effect, and these claims thus cover any compound within the generic scope of the claims, regardless of its activity or use.

The asserted claims are Claims 1, 2, 9, 19, 20, 22, 23 and 24.

A. Basic Chemical Nomenclature

The main issue in the case is whether Ranbaxy's ANDA generic product, which contains a combination of cilastatin sodium and imipenem, infringes any valid claim of the '868 patent.[3] Cilastatin is described in Merck's product insert for PRIMAXIN I.V. (A2496), which contains the combination of imipenem and cilastin, and is identified by the following structural formula,

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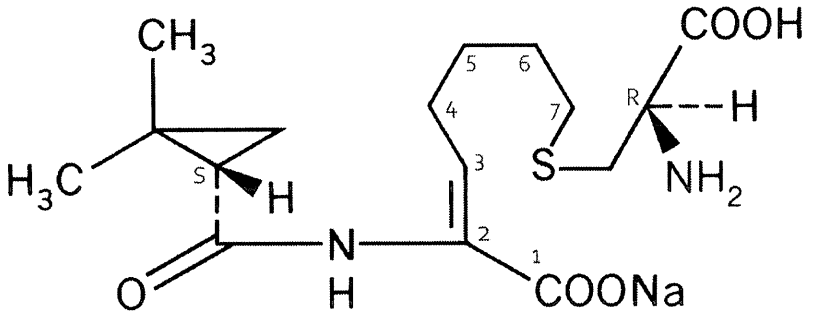
[1] Citations to the '868 patent are given throughout by reference to column and line number.

[2] Intrinsic and extrinsic evidence documents which establish and/or support the facts and positions set forth herein are provided in the parties' Joint Appendix and referenced throughout by "A_" page number designations.

[3] Ranbaxy does not propose that the claims be construed in view of the product accused of infringement, or Merck's commercial embodiment, but instead submits that Merck's description of cilastatin sodium is relevant to the construction of Claims 1, 9, 19, 20 and 21 as discussed below.

in which the 7 carbon atoms of the heptenoate moiety and the chiral centers ("R" and "S") are labeled for purposes of clarity of the following discussion:[4]



Cilastatin sodium is described by Merck in this product insert as "the sodium salt of a derivatized heptenoic acid. Its chemical name is sodium (Z)-7-[[(R)-2-amino-2-carboxyethyl]thio]-2-[(S)-2,2-dimethylcyclopropanecarboxamido]-2-heptenoate." (A2496). Cilastatin sodium is thus a heptenoate sodium salt which has a 7-carbon chain with a double bond between the carbons at the 2- and 3-positions of the heptenoate group (hence, "2-heptenoate"). (A2598).

Cilastatin sodium is also substituted at the 2-position of the heptenoate carbon chain with what Merck describes as an "(S)-2,2-dimethylcyclopropanecarboxamido" group, which is the moiety in the above formula having a three-carbon ring substituted with two CH_3 groups ("dimethyl"). Cilastatin sodium is substituted at the 7-position of the heptenoate carbon chain with an -[(R)-2-amino-2-carboxyethyl]thio group, *i.e.*, the -S-CH_2-$CHNH_2$-COOH moiety in the structural formula above.

Both the 7-[[(R)-2-amino-2-carboxyethyl]thio] substituent and the "2-[(S)-2,2-dimethylcyclopropanecarboxamido]" moiety have one chiral center each, which are designated as "R" and "S", respectively. These designations ("R") and "(S)" denote the specific spatial

[4] For the convenience of the Court, attached as Exhibit A is a glossary of terms defining and explaining relevant organic chemistry nomenclature. Support for the same is provided in the parties' Joint Appendix as referenced in the in the glossary. Ranbaxy is not seeking construction of the terms in the glossary; rather, the glossary is provided simply as background information.

configurations (arrangements in three-dimensional space) at the two chiral carbons. These three-dimensional configurations are shown by the dotted line bonds and the bolded bonds in the structural formula. Some basic aspects of stereochemistry are discussed below for the Court's convenience.

No claim in the '868 patent is specific to cilastatin sodium.

B. Basic Principles Of Stereochemistry Relating To The '868 Patent

Stereochemistry is described using a special and unique nomenclature which the `868 Patent uses. Chemists have followed the same well-established general conventions in using this nomenclature for at least the last two decades. These concepts are briefly discussed in *Pfizer, Inc. v. Ranbaxy Labs. Ltd.*, 457 F.3d 1284, 1286-87 (Fed. Cir. 2006).

Stereoisomers are compounds that are identical except for the way in which their atoms are oriented in space. *See* R.T. Morrison & R.N. Boyd, *Organic Chemistry*, Ch. 4, at 123 (4th ed. 1983) ("*Morrison & Boyd*") (A2606); D.C. Neckers and M.P. Doyle, *Organic Chemistry*, Ch. 9, at 226 (1977) ("*Neckers & Doyle*") (A2583).

Chemists refer to a pair of stereoisomers that are non-superimposable mirror images of each other as "enantiomers."[5] *Morrison & Boyd* at 134 (A2617); *Neckers & Doyle* at 226 (A2583). Enantiomers are often referred to as "optical isomers" because they are optically active, i.e., they rotate the plane of polarized light.

Following general conventions of stereochemistry, chemists distinguish optical isomers (or specific portions of more complex compounds containing more than one "chiral center", as discussed below) based on the three-dimensional spatial arrangement, or configuration, of their atoms, using the symbols "S" and "R". *Morrison & Boyd* at 138-141 (A2621-2624); *Neckers & Doyle* at 237-

[5] Chemists describe this property as "chirality" from the Greek word for "hand" - because, like a person's right and left hands, substances exhibiting this property are non-superimposable mirror images. *See Morrison & Boyd* at 131-132 (A2614-2615).

244 (A2594-2601). Chemists also distinguish graphically between the spatial arrangement of the atoms in optical isomers by using a solid wedge (*e.g.*, indicated at each of "R" and "S" in the dimethylcyclopropyl group in the formula above) to depict a group of atoms that is oriented toward the viewer and a hatched wedge or dotted line (*e.g.*, indicated at each of "R" and "S" in the formula above) to depict a group of atoms that is oriented away from the viewer. *See, e.g.*, D.A. McQuarrie & P.A. Rock, *General Chemistry* at 1071 (3rd ed. 1991) (A2570-2572).

Another method of designation of configuration uses a "Fischer projection" for certain classes of compounds (or portions of larger compounds), such as amino acids and carbohydrates. Under this system, the isomers are distinguished based on the spatial arrangement of their atoms using the symbols "L" and "D" (*see, e.g.*, claims 18-19 of the '868 patent). *Neckers & Doyle* at 237-241 (A2594-2598).

Chemists also distinguish optical isomers based on their optical activity, i.e., in what direction they rotate the plane of polarized light. *Morrison & Boyd* at 126 (A2609); *Neckers & Doyle* at 232-235 (A2589-2592). Following general conventions of stereochemistry, chemists describe the optically active compound that rotates the plane of polarized light to the right, or in a clockwise direction, as dextrorotatory and commonly represent it with a "(+)" symbol or the prefix "*d*-" for "dextro-." Chemists distinguish such compounds from the optically active isomer that rotates the plane of polarized light to the left, or in a counterclockwise direction, which they describe as levorotatory and commonly represent with a "(-)" symbol or the prefix "*l*-" for "levo-." *See* generally, *Morrison & Boyd* at 126-127 (A2609-2610); *Neckers & Doyle* at 232-235 (A2589-2592). The levo- and dextrorotatory isomers are mirror images of each other, i.e., enantiomers.

A complete name for an optical isomer reveals both its configuration ("R" or "S") and the direction in which it rotates polarized light ("(-)" or "(+)"). *Morrison & Boyd* at 139 (A2622).

When chemists synthesize an organic compound that can exist as optical isomers or enantiomers in "R" and "S" configurations, what they obtain will typically contain equal amounts

of each optical isomer. Chemists refer to a substance containing equal amounts of two optical isomers as a "racemate" or "racemic" and commonly represent it with a "(±)" or "(RS)" symbol. *See Morrison & Boyd* at 135, 139 (A2618, A2622) (noting that the "(±)" and ("RS") symbols are used to represent a racemate); *Neckers & Doyle* at 235 (A2592) (same). In depicting the structure of a racemate, chemists do not use a solid or hatched wedge at the relevant location because it can depict only one of the isomers. Instead, they use a straight (\) or wavy (~) line. A racemate does not rotate the plane of polarized light, and is therefore not optically active, because the rotation caused by the levorotatory (-) molecules will be cancelled by the equal and opposite rotation caused by the *precisely same* number of oppositely oriented dextrorotatory (+) molecules. *Morrison & Boyd* at 135 (A2618).

Chemists use the symbols "S" or "R" to represent the three-dimensional configuration at each "chiral" carbon atom (i.e., chiral center -- *see Morrison & Boyd* at 131-133 (A2614-16)) of a compound. A compound with two chiral centers will have four isomers designated (R, R), (S, S), (R, S), or (S, R). Isomers having (R, R) and (S, S) configurations are mirror images of each other (enantiomers). The other combinations of isomers, such as (R, S) and (R, R) are not mirror images and are called diastereomers. *Morrison & Boyd* at 141-143 (A2624-26)

As explained below, some of the compounds of the '868 patent are enantiomers or diastereomers, while others are the racemates.[6] The compounds of certain claims are also designated as having the Z-configuration, based on the nomenclature convention of J.E. Blackwood et al., *J. Amer. Chem. Soc.*, 90, 509 (1968) (A2494-2495), as referenced in the '868 patent (5:7-10) (A4).

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[6] Some slides depicting these general concepts based on the above citations have been included in the Joint Appendix should the Court desire a basic tutorial at the Markman hearing. *See* (A2652-2661).

II. TERMS THAT ARE NOT IN DISPUTE

The parties agree that the term "witho" in Claim 22 should be construed as proposed in the amended Joint Claim Construction Chart.

III. TERMS HAVING A COMMON AND ORDINARY MEANING

The parties failed to reach agreement that certain common chemical terms in the claims have a common, ordinary, and art-recognized meaning. Merck unreasonably refused to stipulate as to the scope of certain limitations, although it does not appear to dispute their common meaning. The definitions of these terms are relevant to Ranbaxy's invalidity defenses based on the lack of written description of the generic subject matter, that is required by 35 U.S.C. §112, first paragraph. Construction of these terms by the Court is necessary to preclude Merck from asserting, at a later stage of the litigation, that they have an uncommon, narrower meaning based on the deficient disclosure of the specification. It begs the question to state that terms should be construed in accordance with their "ordinary meaning," or that the limitations "require no construction," without setting forth a specific, alternative definition or providing reasons why Ranbaxy's proposed construction is not an apparent and ordinary, common meaning to one skilled in the art.

A. R2 is "X" (Claim 1)

1. Ranbaxy's proposed construction

Although R2 is more broadly defined, when R2 is X, Ranbaxy submits that according to the plain language of Claim 1, X includes at least the following groups:

> a branched or linear alkyl group of four carbons substituted with a cycloalkyl group of six carbons (*i.e.*, a cyclohexyl group),
>
> a branched or linear alkyl group of five carbons substituted with a cycloalkyl group of five carbons (*i.e.*, a cyclopentyl group),
>
> a branched or linear alkyl group of six carbons substituted with a cycloalkyl group of four carbons (*i.e.*, a cyclobutyl group), and

a branched or linear alkyl group of seven carbons substituted with a cycloalkyl group of three carbons (*i.e.*, a cyclopropyl group).

2. Intrinsic support for Ranbaxy's construction

Ranbaxy's construction is supported by the language of claim 1, which describes X as including, *inter alia*, "substituted branched or linear alkyl of three to ten carbon atoms" where "said substituents are selected from the group consisting of . . . cycloalkyl of three to six carbon atoms, with the proviso that, when said alkyl is substituted by said cycloalkyl, X is not more than ten total carbon atoms. . . ."

3. Merck's proposed construction

Merck states that "'X' needs no construction" and merely repeats the language of the claim.

4. Reasons why Ranbaxy's construction should be adopted

Ranbaxy's proposed construction simply defines the full range of alkyl groups substituted by cycloalkyl groups that are literally encompassed by this claim language, and gives the claim limitation its ordinary meaning to persons skilled in the art. In the absence of any limiting definition in the specification, this is the construction that should be given to "X." *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005); *Scriptgen Pharms., Inc. v. 3-Dimensional Pharms, Inc.*, 79 F. Supp. 2d 409, 418 (D. Del. 1999). It is Ranbaxy's position that this scope is not supported by the written description of the specification as required by 35 U.S.C. §112, first paragraph, and that Claim 1 is therefore invalid for lack of support.

It appears that there is no dispute as to the broadest reasonable scope of X in Claim 1, and in the absence of a specific, narrower construction proposed by Merck, Merck should be precluded from later asserting any narrower scope of the limitation X.

B. R2 is "Y" (Claim 1)

1. Ranbaxy's proposed construction

Although R2 is more broadly defined, Ranbaxy submits that when R2 is Y, by the plain language of Claim 1, Y includes at least the following groups:

cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl, unsubstituted or substituted with one or two substituents including alkyl of one to four carbon atoms, provided that the total number of carbon atoms in substituted Y is not more than ten carbon atoms.

2. Merck's proposed construction

Merck states that "'Y' needs no construction" and merely repeats the language of the claim.

3. Intrinsic support for Ranbaxy's construction

Ranbaxy's construction is supported by the language of claim 1, which describes Y as including, *inter alia*, "cycloalkyl of three to six carbon atoms. . . substituted with one or two substituents where said substituents are selected from the group consisting of . . . alkyl of one to four carbon atoms, with the proviso that, when said cycloalkyl is substituted by said alkyl, Y is not more than ten total carbon atoms. . . ."

The specification contains no general definition of alkyl, or of the specific alkyl substituents when R^3 is Y. Claim 1 does contain specific definitions of alkyl groups, including straight, branched or cyclic alkyl groups, and nothing in the definition of Y or the description of Y in the specification excludes any of the alkyl groups recited in Claim 1.

4. Reasons why Ranbaxy's construction should be adopted

Ranbaxy's proposed construction simply defines the full range of alkyl groups substituted by cycloalkyl groups that are literally encompassed by this claim language, and gives the claim

limitation its ordinary meaning. Each of the four recited cycloalkyl groups may be substituted with one or two alkyl straight chain, branched chain or cyclic alkyl groups, having up to 4 carbons each, provided that the total number of carbons in Y is at most 10 carbons. For example, when Y is a cyclopropyl group having 3 carbon atoms, it may be substituted with one alkyl group that may have one carbon, two carbons, three carbons (straight, branched or cyclic) or four carbons (straight, branched or cyclic), and with a second alkyl group that may have one carbon, two carbons, or three carbons (straight, branched or cyclic). The cyclic alkyl substituents may similarly be substituted with other alkyl groups, within the definition of Y. Similar combinations are encompassed by the definition of Y when Y is cyclobutyl (4 carbons), cyclopentyl (5 carbons) or cyclohexyl (6 carbons), provided that the total number of carbon atoms in substituted Y is not more than ten carbon atoms.

It is Ranbaxy's position that this scope is not supported by the written description of the specification as required by 35 U.S.C. §112, first paragraph, and that the claim is therefore invalid for lack of support.

It appears that there is no dispute as to the broadest reasonable scope of Y in Claim 1, and in the absence of a specific, narrower construction proposed by Merck, Merck should be precluded from later asserting any narrower scope of the limitation Y.

C. R^3 Substituents (Claim 1)

1. Ranbaxy's Proposed Construction

In Claim 1, the terminal carbon atom of the alkyl group R^3 can be substituted by a number of "moieties" which contain additional alkyl groups. These moieties include the following substituents relevant to Ranbaxy's defenses in this case:

trialkylammonium,

quaternary hydroxyalkyldialkylammonium,

phosphonylalkylamino,

hydroxyalkylamino,

alkylamidino,

N,N-dialkylguanidino,

alkylcarbonyloxy, and

alkoxycarbonyl.

The only claim construction issue relating to these moieties is the definition of "alkyl" that is included in each R^3 substituent. Ranbaxy submits that this term should be construed as follows:

> "Each alkyl group in each substituent includes a linear, branched, or cyclic alkyl group without limitation as to number of carbon atoms."

2. Intrinsic support for Ranbaxy's construction

The '868 patent contains no general or limiting definition of the term "alkyl," and indeed, contains no disclosure of any of the specific R^3 substituents listed above or any definition of the alkyl group or groups contained in each.

3. Reasons why Ranbaxy's construction should be adopted

In the absence of any more specific definitions of these groups, which are not supported by the written description of the specification as required by 35 U.S.C. §112, first paragraph, Ranbaxy's proposed construction is supported by the varying use of the term "alkyl" in Claim 1, and by the specification description of alkyl groups included in other R^3 substituents. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1314 (Fed. Cir. 2005) (claims themselves provide substantial guidance as to the meaning of particular claim terms, in the context of surrounding words of the claim); *Scriptgen Pharms., Inc. v. 3-Dimensional Pharms, Inc.*, 79 F. Supp. 2d 409,

418 (D. Del. 1999) (where a term is not defined in the specification, its ordinary meaning should control).

It is evident from Claim 1 that "alkyl" as used in the claim encompasses at least alkyl groups having as few as one carbon and as many as fifteen carbons, because various alkyl groups recited in the claim are expressly described as being, *e.g.*, "said one to fifteen carbon alkyl," "dialkylamino of one to four carbons per alkyl substituent," "one to four carbon alkylamino, "L-2-amino-2-carboxyethylthio" (in which the alkyl group contains 2 carbons), and "N-methyl-N-carboxymethylamino" (in which each alkyl group contains one carbon). It is clear from the specification the term "alkyl" without further qualification encompasses straight chain alkyl, branched chain alkyl, cyclic alkyl, and cyclic alkyl substituted with other alkyl groups. (*e.g.*, 2:11-13, 2:23-30; 2:34-45, and the examples of alkyl groups in Table I).

In the absence of a limiting definition in the claim, or in the specification, for the alkyl groups of the substituents in question, Ranbaxy submits that the term "alkyl" in the substituents listed above, which is not qualified or modified, should be given its broad, ordinary and common meaning. *See Innova/Pure Water, Inc. v. Safari Water Filtration Sys.*, 381 F.3d 1111, 1118 (Fed. Cir. 2004) (in the absence of modifiers, general descriptive terms are typically construed as having their full meaning)

D. "R^2" (Claim 22)

1. Ranbaxy's proposed construction

Although R^2 is more broadly defined in Claim 22, Ranbaxy submits that the plain language of Claim 22, R^2 in Claim 22 includes at least the following groups:

cyclopropyl substituted by two substituents of one, two, or three carbon atoms each;

cyclobutyl substituted by two substituents of one, two, or three carbon atoms each;

cyclopentyl substituted by one substituent of one, two, or three carbon atoms and by one substituent of one or two carbon atoms; and

cyclohexyl substituted by one substituent of one, two, or three carbon atoms and by one substituent of one carbon atom, or cyclohexyl substituted by one substituent of one or two carbon atoms and by one substituent of one or two carbon atoms.

2. Merck's proposed construction

Merck states that "'R^2' needs no construction" and suggests no alternative definition, and merely repeats the language of the claim.

3. Intrinsic support for Ranbaxy's construction

Ranbaxy's construction is supported by the language of claim 22, which describes R^2 as including, *inter alia*, "cycloalkyl of three to six carbon atoms substituted by two alkyl substituents of one to three carbon atoms each, with the proviso that R2 cannot contain more than ten carbon atoms."

4. Reasons why Ranbaxy's construction should be adopted

Ranbaxy's proposed construction simply defines the full range of alkyl groups substituted by cycloalkyl groups that are literally encompassed by this claim language, and gives the claim limitation its ordinary meaning. It is Ranbaxy's position that this scope is not supported by the written description of the specification as required by 35 U.S.C. §112, first paragraph, and that the claim is therefore invalid for lack of support. For the same reasons as above with respect to the limitation "Y", alkyl substituents without further qualifiers or modifiers include all forms, *i.e.*, straight, branched and cyclic or substituted cyclic. *See Innova/Pure Water, Inc. v. Safari Water Filtration Sys.*, 381 F.3d 1111, 1118 (Fed. Cir. 2004).

It appears that there is no dispute as to the broadest reasonable scope of R^2 in Claim 22, and in the absence of a specific, narrower construction proposed by Merck, Merck should be precluded from later asserting any narrower scope of the limitation R^2.

E. "2,2-dimethylcyclopropyl" (Claims 2 and 9)

1. Ranbaxy's Proposed Construction

Claims 2 and 9 recite that R^2 is or includes " 2,2-dimethylcyclopropyl." Ranbaxy submits that this term should be construed as follows:

"(S)-2,2-dimethylcyclopropyl, (R)-2,2-dimethylcyclopropyl, and mixtures thereof"

2. Intrinsic support for Ranbaxy's construction

In the list of compounds according to the invention in Table I, Compounds 2, 2a and 2b, *i.e.*, 2-butenoic acids in which R^2 is a 2,2-dimethylcyclopropyl group, "are the racemic, dextrorotatory and levorotatory forms respectively." (19:34). The terms "dextrorotatory" and "levorotatory" describe the direction in which the two enantiomers rotate polarized light.

With respect to other enantiomer forms and mixtures thereof, the specification states as follows (2:18-22):

> Some of the compounds with formula II [*sic*] above have asymmetric forms. Racemic Z-2-(2,2-dimethylcyclopropanecarboxamido)-2-octenoic acid has been resolved. The activity resides in the dextrorotatory isomer, which has the S-configuration.

3. Reasons why Ranbaxy's construction should be adopted

The specification makes it clear that compounds 2, 2a and 2b with R^2 substituent 2,2-dimethylcylopropyl have two R and S configurations, which result in enantiomeric forms of the compound, described as the dextrorotatory and levorotatory forms, and as a racemate containing the two enantiomers. Based on the clear intrinsic disclosure of the two enantiomers and racemate of these compounds containing the 2,2-dimethylcyclopropyl substituent, the term "2,2-dimethylcyclopropyl" should be construed to include both R and S configurations, and mixtures thereof.

IV. CLAIM TERMS IN DISPUTE

A. "A compound" (Claims 1 and 9)

1. Ranbaxy's Proposed Construction

Claims 1 and 9 recite "a compound" of the structural formula. Ranbaxy submits that this term should be construed as follows:

> "'A compound' excludes a combination product containing the compound and a thienamycin-type compound."

2. Intrinsic support for Ranbaxy's construction

Ranbaxy's proposed construction is supported by the clear and unambiguous disclaimer of a combination product in the '868 patent specification, at (8:43-60), which states as follows:

> As mentioned above, the thienamycin-type compound is used in combination with the dipeptidase inhibitor. *The combination product is not part of this invention, but is claimed in a copending application*, Case 16174, U.S. Ser. No. 927,213, filed Jul. 24, 1978, now abandoned, and in Case 16174IA, U.S. Ser. No. 050,232, filed Jun. 22, 1979, now abandoned, and in Case 16174IB, filed concurrently herewith. (emphasis added).
>
> The combination of *the novel chemical inhibitors of this invention* and the thienamycin class compound can be in the form of a pharmaceutical composition containing the two compounds in a pharmaceutically acceptable carrier. The two can be employed in amounts so that the weight ratio of the thienamycin class compound to inhibitor is 1:3 to 30:1, and preferably 1:1 to 5:1.

This language is also found in prior patent Application Serial Nos. 05/927,212 (A36-37), 06/50,233 (A119), 06/465,577 (A363), 06/748,300 (A478), 06/878,391, 07/244,527, 07/641,317 and 07/839,725 listed on the face of the '868 patent.[7]

3. Additional support for Ranbaxy's construction

U.S. Patent No. 4,539,208 (expired) contains claims directed to a combination of a dipeptidase inhibitor with a thienamycin compound. (A2000-21). In addition, Application Serial Nos. 05/927,213 (A2462-67), 06/50,232 (A2376-80), 06/187,929 (A2276-81) and 06/291,711

[7] The last four listed applications were continuations under former 37 C.F.R. §1.62, which used the specification from the '300 application.

(A2101-06) leading to the issuance of the '208 patent also contain combination claims and are relied upon for support.

4. Reasons why Ranbaxy's construction should be adopted

The disclaimer language used in the '868 patent reflects a clear and unequivocal decision by Merck to simultaneously pursue -- in separate patent applications -- patent protection for dipeptidase inhibitors and a combination of a dipeptidase inhibitor with a thienamycin compound. The disclaimer language was not added during prosecution for clarification of an ambiguous patent scope, it was not added in response to any prior art asserted by the Patent Office, and it was not in response to any rejection of any claim during prosecution of any of the applications leading to the '868 patent. Merck's strategy was to seek protection of cilastatin *separately* from a cilastatin-imipenem combination product in *unrelated* patents. Other patents in the '208 patent combination family stemming from the original Application Ser. No. 05/927,213 include U.S. Patent Nos. 4,880,793 (expired), and 4,161,038 (expired). Merck never updated the original disclosure of abandoned Application Ser. Nos. 927,213 and 050,232 ('868 patent 8:43-51), to bring these copending applications and issued patents to the attention of the examiner.[8]

On July 24, 1978, Merck filed two patent applications at the U.S. Patent Office that were given sequential application serial numbers. U.S. Application No. 927,212 contained claims to certain dipeptidase inhibitors (e.g., cilastatin) (A71-75) and U.S. Application No. 927,213 contained claims directed to combinations of dipeptidase inhibitors with thienamycin compounds (A2462-67). Merck's '212 application disclaimed a claim scope that included the combination

[8] During prosecution of the applications leading to the '868 patent in suit, Merck failed to disclose to the PTO the existence of the copending applications that issued as these expired combination patents, and also failed to disclose the issuance of the patents themselves to the examiners responsible for examining the applications leading to the '868 patent.

product, and that disclaimer language was contained in each and every application leading to the issuance of the '868 patent, as shown above. Merck's strategy of delaying the present dipeptidase claims, and failing to disclose the combination claims, was successful. The asserted '868 patent claiming dipeptidase compounds issued in 1992 and is set to expire in 2009. (A1). The '208 patent (directed to combinations of compounds) issued in 1985 and expired in 2002 (A2000). For over fifteen years, the public has relied on Merck's representation in the '868 patent as to the proper scope of each patent. Indeed, Ranbaxy did not seek approval of any imipenem-cilastatin combination product while the '208 combination patent was in force. Now, almost thirty years after Merck's strategic decision to protect the combination product and a compound of the combination product separately, Merck takes the opposite position -- that the disclaimer language in the '868 patent is not a disclaimer, and does not exclude the combination product from the scope of the '868 patent claims. Merck's current interpretation cannot erase the clear disclaimer language of the patent, its own thirty-year old strategic decision, and decades of public reliance on that decision.

In construing claims, the specification is examined to determine if the patentee has limited the scope of the claims. *Watts v. XL Sys., Inc.*, 232 F.3d 877, 882 (Fed. Cir. 2000). Where the specification makes clear that the invention does not include a particular feature, that feature is deemed to be outside the reach of the claims of the patent, even though the language of the claims, read without reference to the specification, might be considered broad enough to encompass the feature in question. *SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1341 (Fed. Cir. 2001); *Cultor Corp. v. A.E. Staley Mfg. Co.*, 224 F.3d 1328, 1331 (Fed. Cir. 2000) ("Claims are not correctly construed to cover what was expressly disclaimed.").

Here, the disclaimer language in the '868 patent is not only relevant to claim scope, it is dispositive. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1315 (Fed. Cir. 2005) (*en banc*) ("the specification 'is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term.'"), quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). In *Phillips*, the Federal Circuit explained that "the specification may reveal an intentional disclaimer, or disavowal, of claim scope by the inventor. In that instance as well, the inventor has dictated the correct claim scope, and the inventor's intention, as expressed in the specification, is regarded as dispositive." *Id.* at 1316.

Before and after *Phillips*, courts have freely found a disclaimer of claim scope where the language was both clear and intentional. *See SciMed Life Sys.*, 242 F.3d at 1345 ("[b]ecause the three *SciMed* patents make clear that the lumens referred to in the claims are all coaxial in structure, the district court was correct to construe the patents as disclaiming the dual lumen configuration"); *Wang Labs, Inc. v. America Online, Inc.*, 197 F.3d 1377, 1382 (Fed. Cir. 1999) (although the claim term "frame" could be applied both to "bit-mapped display systems" and to "character-based systems," the court construed the claims as limited to character-based systems as the "only system that is described and enabled" in the patent specification.); *Cultor Corp,* 224 F.3d at 1331 (Where the written description explicitly limited the subject matter of the patent to a polydextrose purification process using a citric acid catalyst, the court declined to hold that the asserted claims read on a process using a catalyst other than citric acid, even though the claims themselves did not refer to citric acid. The explicit reference in the specification to the invention as a process limited to one prepared with the citric acid catalyst had "effected a disclaimer of the other prior art acids.").

In *SafeTCare Mfg., Inc. v. Tele-Made, Inc.*, 497 F.3d 1262 (Fed. Cir. 2007), the court upheld a summary judgment grant of noninfringement based on a claim construction that excluded the accused product from claim scope because of the disclaimer in the patent specification. At issue was whether Claim 12 of the asserted patent directed to a bariatric bed encompassed a plurality of motors that exerted *pulling* forces (in addition to *pushing* forces) on a bracket, called a "lift dog." The court considered statements in the Background, Summary of the Invention and Detailed Description sections of the patent that repeatedly emphasized that the motor of the patented invention applied a *pushing* force against the lift dog. Combined with the inventor's emphasis of that attribute as important in distinguishing over the prior art, the court concluded that the patentee's language disclaimed motors that use *pulling* forces against lift dogs:

> As described by the patentee in the statements included above, the patentee disavowed such motors from the limitation in Claim 12 covering motors "exerting a pushing force on . . . deck sections." We follow *Phillips* and hold that the patentee's disavowal of such motors in the specification is dispositive. *Id.* at 1270-71.

Merck's clear and intentional statement in the '868 patent presents an even more compelling case of disclaimer than that in any of the foregoing cases, by affirmatively stating what is ***not*** part of the invention rather than simply what ***is*** included. Under these circumstances, the scope of Claim 1 does not, and cannot, include a thienamycin-type compound when combined with a dipeptidase inhibitor.

B. The structural formula (Claims 1 and 9)

1. Ranbaxy's Proposed Construction

Claims 1 and 9 define the compound with reference to a structural formula. Ranbaxy proposes that the structural formula in Claim 1 should be construed to have the full scope of its ordinary meaning, as follows:

> "The formula includes racemates, mixtures, isomers, and enantiomers of the free acid form and salt forms of the compound, with the exception of the E-stereoisomer form."

Putting aside the R group definitions addressed elsewhere, Ranbaxy proposes that the structural formula in Claim 9 should be construed to have the full scope of its ordinary meaning, as follows:

> "The formula includes racemates, mixtures, isomers, and enantiomers of the free acid form, salt forms, and ester forms of the compound, with the exception of the E-stereoisomer form."

2. Intrinsic support for Ranbaxy's construction

The '868 patent specification does not provide a definition of the structure of the generic structural formula, except to state that the compounds of the invention "include" chemical compounds having the Z stereoconfiguration. (1:47-59). The specification does not provide a description of all isomers included in the generic structural formula, depending on the selection of particular substituents.

With respect to enantiomer forms and mixtures thereof, the specification states as follows (2:18-22):

> Some of the compounds with formula II [*sic*] above have asymmetric forms. Racemic Z-2-(2,2-dimethylcyclopropanecarboxamido)-2-octenoic acid has been resolved. The activity resides in the dextrorotatory isomer, which has the S-configuration.
> In the list of compounds according to the invention in Table I, Compounds 2, 2a and 2b,

which are 2-butenoic acids in which R^2 is a 2,2-dimethylcyclopropyl group, "are the racemic, dextrorotatory and levorotatory forms respectively." (19:34). The terms "dextrorotatory" and "levorotatory" describe the direction in which the respective enantiomers rotate polarized light.

Furthermore, the specification discloses "7-(L-2-amino-2-carboxyethylthio)-2-(2,2-dimethylcyclopropanecarboxamido)-2-heptenoic acid" (5:3-6), which is the compound claimed in Claim 19. In this compound, "L" indicates that the chiral center in the 2-amino-2-carboxyethylthio substituent has the R configuration. In other cases, the specification uses

different terms to describe optically active isomer forms, such as the R^2 group shown in Example 66 of Table 1, designated as having the (+) configuration.

3. Reasons why Ranbaxy's construction should be adopted

"Asymmetric forms" of compounds claimed in the '868 patent are enantiomeric forms having chiral centers, and the disclosed Z-2-(2,2-dimethylcyclopropanecarboxamido)-2-octenoic acid has a chiral center in the 2,2-dimethylcyclopropanecarboxamido substituent. The "racemic" acid or "racemate" of this compound is an equal mixture of the S-enantiomer and the R-enantiomer of this acid. A racemic mixture is "resolved" by separating the S-enantiomer and the R-enantiomer. (A2618-2619). The enantiomeric substituents rotate polarized light in either a clockwise (dextrorotatory) or counterclockwise (levorotatory) direction. (A2652-2661, A2611 and A2613-2614).

Ranbaxy's proposed construction, which encompasses all isomers, including enantiomers and mixtures thereof of compounds within the structural formula, is supported by the specification which identifies the racemate and the dextrorotatory and levorotatory enantiomers of Compounds 2, 2a and 2b in Table I, and the (+) (dextrorotatory) enantiomer of Compound 66. With respect to Claim 19, the 7-(L-2-amino-2-carboxyethylthio) substituent has the R-configuration, but the claim does not specify the R- or S- configuration of the 2,2-dimethylcyclopropanecarboxamido moiety. Thus, Claim 19 encompasses both isomers and mixtures thereof.

In the absence of any narrowing definition in the specification, the structural formula should be construed to include all isomers, enantiomers, racemic and other mixtures of Z-stereoisomer compounds within the scope of the structural formula in Claims 1 and 9, because this construction gives the claims their full scope when interpreted in view of the specification.

See Pfizer, Inc. v. Ranbaxy Labs., Ltd., 457 F.3d 1284, 1289 (Fed. Cir. 2006) (structural formula depicting a single enantiomer interpreted to include R-isomer, S-isomer or any (equal or unequal) mixtures thereof).

C. "R1" (Claim 1)

1. Ranbaxy's Proposed Construction

Claim 1 recites that "R1 is hydrogen or a pharmaceutically acceptable cation." Ranbaxy submits that this term should be construed as follows:

> "R1 defines two mutually exclusive subgenera: (1) a free acid form in which R1 is hydrogen, and (2) salt forms in which R1 is a pharmaceutically acceptable cation."

2. Intrinsic support for Ranbaxy's construction

Ranbaxy's proposed construction is supported by the clear and unambiguous definition provided in the '868 patent specification (5:11-19):

> Although these compounds of Formula I, when R^1 is H, are described and named as the free acids, it will be apparent to one skilled in the art that various pharmaceutically acceptable derivatives such as alkali and alkaline earth metal, ammonium, or amine salts, or the like can be employed as equivalents thereto. Salts such as the sodium, potassium, calcium, or tetramethylammonium salts are suitable.

3. Reasons why Ranbaxy's construction should be adopted

The specification clearly and unambiguously distinguishes the scope of R1, when R1 is hydrogen and when R1 is a pharmaceutically acceptable cation. When R1 is hydrogen, the compounds are "described and named as the free acids." The term "pharmaceutically acceptable cation" is not expressly defined in the specification, but the specification describes "pharmaceutically acceptable derivatives" in which the disclosed compounds are certain pharmaceutically acceptable salts, including classes of salts ("alkali and alkaline earth metal, ammonium, or amine salts") or specific salt forms ("the sodium, potassium, calcium, or tetramethylammonium salts").

The express definition of R1 in the specification thus clearly distinguishes the free acid compounds of the general formula from salt compounds of the general formula. Compounds in which R1 is H, by definition, cannot be compounds in which R1 is something other than H. The definition of R1 in Claim 1 thus defines two mutually exclusive categories of compounds.

D. "Pharmaceutically acceptable cation" (Claims 1 and 9)

1. Ranbaxy's Proposed Construction

Claims 1 and 9 recite that R1 includes "a pharmaceutically acceptable cation." Ranbaxy submits that this term should be construed as follows:

"Any cation useful in the salt form of the claimed pharmaceutical compound."

2. Intrinsic support for Ranbaxy's construction

The term "pharmaceutically acceptable cation" is not expressly defined in the specification, which describes R^1 as follows (5:11-19):

> Although these compounds of Formula I, when R^1 is H, are described and named as the free acids, it will be apparent to one skilled in the art that various pharmaceutically acceptable derivatives such as alkali and alkaline earth metal, ammonium, or amine salts, or the like can be employed as equivalents thereto. Salts such as the sodium, potassium, calcium, or tetramethylammonium salts are suitable.

3. Reasons why Ranbaxy's construction should be adopted

There appears to be no significant dispute between the parties that "pharmaceutically acceptable cation" is not limited to the specific examples of pharmaceutically acceptable derivatives listed in the '868 patent specification. Ranbaxy seeks the present construction to ensure that Merck does not propose a narrower construction of the term later, in response to Ranbaxy's invalidity argument that the ordinary, full scope of the claim as understood by a person skilled in the art is not supported by a written description required by 35 U.S.C. §112, first paragraph.

E. "Said one to fifteen carbon alkyl" (Claim 1)

1. Ranbaxy's Proposed Construction

Claim 1 contains inconsistent definitions of alkyl groups represented by substituent R^3 in the general formula, and recites both that:

R^3 is "unsubstituted or substituted two to fifteen carbon alkyl" and

R^3 is "said one to fifteen carbon alkyl."

Ranbaxy submits that the term "said one to fifteen carbon alkyl" should be construed to have its plain and literal scope, which is "said one to fifteen carbon alkyl."

2. Intrinsic support for Ranbaxy's construction

Ranbaxy's proposed construction is supported both by the clear and unambiguous description of the claim, and by the disclosure of the specification, which expressly defines R^2 and R^3 in formula I as follows (1:55-61):

> "R^2 and R^3 are hydrocarbon radicals in the range respectively of 3-10 and 1-15 carbon atoms."

There is no description in the specification of R^3 as having a range of "two to fifteen carbon alkyl" as Merck now proposes.

Moreover, the specification is replete with examples in which R^3 is one carbon, *i.e,* a methyl substituent, and the compound of formula I is therefore a 2-butenoic acid compound. By far the majority of specific compounds disclosed in the specification (2:48-4:26) are 2-butenoic acid compounds in which R^3 is one carbon. Furthermore, in Table I, it is also apparent that most of the compounds disclosed are also compounds in which R^3 is a single carbon atom, *e.g.*, compound nos. 2a, 2b, 2c, 3, 5-11, 18-32, 34-38, 40, and 42-44 (cols. 11-16).

Each of the *in vivo* examples of the patent discloses tests of 2-butenoic acid compounds, in which R^3 is one carbon (19:35-21:42). Examples in which R^3 is one carbon include the 2-butenoic acid compounds of Examples 6, 8-10, 12, and 15.

3. Reasons why Ranbaxy's construction should be adopted

Merck now seeks to rewrite Claim 1, by changing the clear and unambiguous limitation "said one to fifteen carbon alkyl" to "said two to fifteen carbon alkyl." Ranbaxy submits that this limitation of the claim should be construed to have its ordinary, plain, and unambiguous meaning, which is clearly "said one to fifteen carbon alkyl."

Ranbaxy's construction is overwhelmingly supported by the disclosure of the specification, which initially defines R^3 as a hydrocarbon radical "in the range . . . of . . . 1-15 carbon atoms" and further illustrates dozens of preferred compounds in which R^3 is a single carbon atom. In contrast, the construction proposed by Merck is not supported by any similar definition in the specification. Indeed, there is no mention in the '868 patent that R^3 can be a "two to fifteen carbon alkyl."

To be sure, the examiner amended Claim 1 at the close of prosecution, and changed one of the two definitions of R^3 to recite that R^3 is "unsubstituted or substituted two to fifteen carbon alkyl." (A844). In making this amendment, the examiner did not point to any specific written description for the artificial subgenus created by this amendment, did not comment on the reasons for the amendment, and did not explain why the remaining, broader definition of R^3 was retained. (A841, 844). Merck authorized the partial amendment of Claim 1. (A844). Although the examiner invited Merck to provide any comments or further amendment that might be required (A844), Merck did not respond. The artificial subgenus carved out of original Claim 1 by this unexplained amendment is not supported by the disclosure of the specification, as required by 35 U.S.C. §112, first paragraph. Under these circumstances, the unexplained amendment of only one clause of claim 1, with Merck's approval, does not require a construction that would deprive the claim of support in the specification. *See Phillips v. AWH Corp.*, 415 F.3d

1303, 1317 (Fed. Cir. 2005) (because the prosecution history is a record of ongoing negotiation, it "it often lacks the clarity of the specification and thus is less useful for claim construction purposes").

The broader remaining definition of R^3 in Claim 1, as a one to fifteen carbon alkyl, plainly is supported by express definition in the specification (1:55-61) and the disclosure of preferred 2-butenoic acid compounds. The Court should not adopt a construction of R^3 that is unsupported by the specification, rather than construction which is clearly supported, regardless of Merck's reasons for amending only part of Claim 1 in response to the examiner's suggestion. *See Scriptgen Pharms., Inc. v. 3-Dimensional Pharms, Inc.*, 79 F. Supp. 2d 409, 418 (D. Del. 1999) (rejecting a claim interpretation that is not supported by the patent specification).

These internally inconsistent definitions render the claim indefinite, and therefore invalid under 35 U.S.C. §112, second paragraph, because a person skilled in the art would not be able to determine whether a compound in which R^3 is a one carbon alkyl, such as those illustrated in the majority of the '868 patent examples, is included in the scope of the claim as a "one to fifteen carbon alkyl" or is excluded because it is not an "unsubstituted or substituted two to fifteen carbon alkyl."

Indefiniteness under §112, second paragraph is a legal conclusion that is drawn from a court's duty to construe claims, and like claim construction is a question of law. *Default Proof Credit Card Sys. v. Home Depot U.S.A., Inc.*, 412 F.3d 1291, 1298 (Fed. Cir. 2005). If the Court adopts Ranbaxy's proposed construction of R^3 the Court should also hold Claim 1 to be invalid based on the existing inconsistent definitions of R^3 in the claim.

Merck appears to suggest that the inconsistent definition of R^3 in Claim 1 is a "typographical error." It is clear, however, that the error is not "typographical" but instead is

substantive, because both definitions are equally clear and equally unambiguous, and the specification clearly supports only the construction that Merck now seeks to eliminate. Merck could have applied for and received a certificate of correction of the '868 patent under 35 U.S.C. §255, which provides for a certificate of correction of applicant's mistake "whenever a mistake of a clerical or typographical nature, or of minor character" appears in a patent, provided that "the correction does not involve such changes in the patent as would constitute new matter or would require reexamination." If the error in claim 1 indeed were "typographical" rather than substantive, Merck could easily have sought to correct the definition of R^3 by a certificate of correction at any time during the '868 patent's fifteen-year history. Merck may not correct a substantive error in the claim under the guise of claim construction, when it clearly could not correct the alleged "error" in the Patent Office by a certificate of correction, without substantive reexamination of the claim.

Even if contrary to fact, the inconsistent definition which is "error" in Claim 1 were apparent on its face, or from the specification, this would not provide a basis for a saving construction of the claim. The Federal Circuit has emphasized that courts "should not rewrite claims to preserve their validity." *Pfizer, Inc. v. Ranbaxy Labs., Ltd.*, 457 F.3d 1284, 1292 (Fed. Cir. 2006), quoting *Nazioni Communications, Inc. v. Arm Holdings, PLC*, 403 F.3d 1364, 1368 (Fed. Cir. 2005). As the Federal Circuit instructed in *Pfizer*, "[i]f the only claim construction that is consistent with the claim's language and the written description renders the claim invalid, then . . . the claim is simply invalid." 457 F.3d at 1292, quoting *Rhine v. Casio, Inc.*, 183 F.3d 1342, 1345 (Fed. Cir. 1999).

Merck now must live with the consequences of allowing Claim 1 to issue with inconsistent definitions of R^3, and failing to seek to correct this supposed "error" in the Patent

Office over the fifteen-plus year life of the '868 patent. With respect to such "semantic indefiniteness," the Federal Circuit has instructed that it is not the function of the court to rewrite the claim, and "it is of no moment that the contradiction is obvious: semantic indefiniteness of claims 'is not rendered unobjectionable simply because it could have been corrected.'" *Allen Eng'g Corp. v. Bartell Indus., Inc.*, 299 F.3d 1336, 1349 (Fed. Cir. 2002), quoting *In re Hammack*, 427 F.2d 1384, 1388 n.5 (C.C.P.A. 1970).

The Federal Circuit has made it plain that claim construction is not a panacea, for patentees who negligently fail to proof their claims prior to litigating them. Even where the plain language of a claim is nonsensical, and this fact is apparent from review of the specification, "courts may not redraft claims, whether to make them operable or to sustain their validity." *Chef America, Inc. v. Lamb-Weston, Inc.*, 358 F.3d 1371, 1374 (Fed. Cir. 2004).

F. "R^1" (Claim 9)

1. Ranbaxy's Proposed Construction

Claim 9 recites that "R^1 is hydrogen, loweralkyl of 1-6 carbon atoms, dialkylaminoalkyl, or a pharmaceutically acceptable cation." Ranbaxy submits that this term should be construed as follows:

> "R^1 defines three mutually exclusive subgenera: (1) a free acid form in which R^1 is hydrogen, (2) ester forms in which R^1 is loweralkyl of 1-6 carbon atoms, or dialkylaminoalkyl, and (3) salt forms in which R^1 is a pharmaceutically acceptable cation."

2. Intrinsic support for Ranbaxy's construction

Ranbaxy's proposed construction is supported by the clear and unambiguous definition provided in the '868 patent specification (5:11-19):

> Although these compounds of Formula I, when R^1 is H, are described and named as the free acids, it will be apparent to one skilled in the art that various pharmaceutically acceptable derivatives such as alkali and alkaline earth metal, ammonium, or

> amine salts, or the like can be employed as equivalents thereto. Salts such as the sodium, potassium, calcium, or tetramethylammonium salts are suitable.

Claim 9 differs from Claim 1, in that the R^1 groups recited in the alternative in Claim 9 include not just (1) hydrogen or (2) a pharmaceutically acceptable cation, but also (3) loweralkyl of 1-6 carbon atoms or dialkylaminoalkyl. The additional R^1 groups are disclosed in the specification (2:15-17) and are esters in which the hydrogen of the free acid (-COOH) is replaced with a lower alkyl group of 1-6 carbon atoms, or with a dialkylaminoalkyl group, *i.e.*, a group containing a nitrogen atom bonded to three carbon atoms. Two dialkylaminoalkyl groups are described in the specification (2:17).

3. Reasons why Ranbaxy's construction should be adopted

The specification clearly and unambiguously distinguishes the scope of R^1, when R^1 is hydrogen, and when R^1 is a pharmaceutically acceptable cation. When R^1 is hydrogen, the compounds are "described and named as the free acids." The term "pharmaceutically acceptable cation" is not expressly defined in the specification, but the specification describes "pharmaceutically acceptable derivatives" in which the disclosed compounds are certain salts, including classes of salts ("alkali and alkaline earth metal, ammonium, or amine salts") and specific salt forms ("the sodium, potassium, calcium, or tetramethylammonium salts"). The specification also provides a description of the scope of R^1, when R^1 is a lower alkyl group of 1-6 carbon atoms or a dialkylaminoalkyl group. (2: 15-17).

The express definition of R^1 in the specification thus clearly distinguishes the free acid compounds of the general formula from salt compounds of the general formula. Compounds in which R^1 is H, by definition, cannot be compounds in which R^1 is something other than H. The definition of R^1 in Claim 9 thus delineates three mutually exclusive categories of compounds, in which R^1 is (1) a free acid (R^1 is hydrogen), or (2) a salt compound (R^1 is a pharmaceutically

acceptable cation, *i.e.*, a salt), or (3) an ester compound (R^1 is loweralkyl of 1-6 carbon atoms or dialkylaminoalkyl). There is no compound which can be both a free acid, in which R^1 is defined as hydrogen, and also an ester compound or a salt compound, because in these other alternative forms R^1 necessarily excludes hydrogen.

The claim construction issue with respect to R^1 in Claim 9 is thus straightforward, because R^1 defines in the alternative three mutually distinct subgenera of compounds, which have no members in common and which cannot overlap.

G. The heptenoic acid compound (Claim 19)

1. Ranbaxy's Proposed Construction

Claim 19 recites "The compound of claim 9 which is 7-(L-2-amino-2-carboxyethylthio)-2-(2,2-dimethylcyclopropanecarboxamido)-2-heptenoic acid." Ranbaxy submits that this term should be construed as follows:

> "the free acid form of 7-(L-2-amino-2-carboxyethylthio)-2-(2,2-dimethylcyclopropanecarboxamido)-heptenoic acid, excluding a pharmaceutically acceptable cation,
>
> the free acid form including the (S)-(2,2-dimethylcyclopropanecarboxamido) form, the (R)-(2,2-dimethylcyclopropanecarboxamido) form, and mixtures thereof."

2. Intrinsic support for Ranbaxy's construction

Claim 19 depends from Claim 9, and further specifies that the claimed compound is the free heptenoic acid, in which R^1 is hydrogen, *i.e.*, the first of the three subgenera defined in the alternative by Claim 9, which recites that R^1 is hydrogen, loweralkyl of 1-6 carbon atoms, dialkylaminoalkyl, or a pharmaceutically acceptable cation.

The specification clearly and unambiguously distinguishes the free acid from other derivatives of compounds of the general formula as follows (5:11-19):

> Although these compounds of Formula I, when R1 is H, are described and named as the free acids, it will be apparent to one

> skilled in the art that various pharmaceutically acceptable derivatives such as alkali and alkaline earth metal, ammonium, or amine salts, or the like can be employed as equivalents thereto. Salts such as the sodium, potassium, calcium, or tetramethylammonium salts are suitable.

Claim 19 does not include derivatives such as pharmaceutically acceptable salts of 7-(L-2-amino-2-carboxyethylthio)-2-(2,2-dimethylcyclopropanecarboxamido)-2-heptenoic acid, which are separately recited in independent Claim 9.

With respect to asymmetric forms of other compounds having a 2,2-dimethylcyclopropanecarboxamido group at the 2-position, the specification states as follows (2:18-22):

> Some of the compounds with formula II [*sic*] above have asymmetric forms. Racemic Z-2-(2,2-dimethylcyclopropanecarboxamido)-2-octenoic acid has been resolved. The activity resides in the dextrorotatory isomer, which has the S-configuration.

3. Reasons why Ranbaxy's construction should be adopted

In view of the clear and unambiguous language of dependent Claim 19, Claim 19 should be construed to encompass only the free heptenoic acid, and not pharmaceutically acceptable salts or esters which are recited as alternative classes of compounds in independent Claim 9. Given the absence of "pharmaceutically acceptable salts" in dependent Claim 19, the intrinsic evidence precludes an interpretation of the term "heptenoic acid" in dependent Claim 19 which could include heptenoate salts. This claim construction issue, which is a pure question of law based on the grammatical structure of the claims, including an independent claim which recites alternative, mutually exclusive groups and a dependent claim which recites only one of the groups, is governed by *Pfizer, Inc. v. Ranbaxy Labs., Ltd.*, 457 F.3d 1284, 1291 n.6 (Fed. Cir. 2006).

In *Pfizer v. Ranbaxy*, the independent claim at issue, like present Claim 9, recited in the alternative (1) atorvastatin acid; or (2) atorvastatin lactone; or (3) "pharmaceutically acceptable salts thereof." 457 F.3d at 1291. Dependent Claim 2 recited only one of the three alternatives,

i.e., "atorvastatin acid." *Id.* The Federal Circuit interpreted Claim 2 to exclude pharmaceutically acceptable salts, because this dependent claim did not contain the "pharmaceutically acceptable salts" language which was used in Claim 1. The intrinsic evidence, *i.e.*, the language of the claims at issue, precluded a broader construction of dependent Claim 2. *Id.*

Under *Pfizer v. Ranbaxy*, in view of the structure and language of Claim 9 and dependent Claim 19, and also in view of the express definition of the free acid that is provided in the specification (5:11-19), Claim 19 should be construed as being limited to the free acid, excluding pharmaceutically acceptable salts that are separately recited in the alternative in Claim 9.

Claim 19 is limited to the 2-heptenoic free acid compound, in which the 7-(L-2-amino-2-carboxyethylthio) group has the R-configuration. However, Claim 19 clearly encompasses both isomeric forms within the scope of the claim, having a 2-(S)-(2,2-dimethylcyclopropane-carboxamido) group or a 2-(R)-(2,2-dimethylcyclopropanecarboxamido) group. Claim 19 should be construed to include these two forms and mixtures thereof, in order to give Claim 19 its full literal scope.

H. The heptenoate salts (Claim 20)

1. Ranbaxy's Proposed Construction

Claim 20 recites "The compound of claim 19 in the sodium, potassium, calcium or magnesium salt form." Ranbaxy submits that the term "the sodium, potassium, calcium or magnesium salt form" should be construed as follows:

"the sodium, potassium calcium or magnesium salt form, excluding the free acid form."

2. Intrinsic support for Ranbaxy's construction

Claim 20 depends from Claim 19, but specifies that the claimed compound is the sodium, potassium, calcium or magnesium salt form, *i.e.*, specific pharmaceutically acceptable salts which are members of the third subgenus defined in the alternative by Claim 9, which recites in

the alternative that R^1 is (1) hydrogen, (2) loweralkyl of 1-6 carbon atoms or dialkylaminoalkyl, or (3) a pharmaceutically acceptable cation.

The specification clearly and unambiguously distinguishes the free acid from salt compounds of the general formula as follows (5:11-19):

> Although these compounds of Formula I, when R1 is H, are described and named as the free acids, it will be apparent to one skilled in the art that various pharmaceutically acceptable derivatives such as alkali and alkaline earth metal, ammonium, or amine salts, or the like can be employed as equivalents thereto. Salts such as the sodium, potassium, calcium, or tetramethylammonium salts are suitable.

3. Reasons why Ranbaxy's construction should be adopted

In contrast to Claim 19, which is limited to the 7-(L-2-amino-2-carboxyethylthio)-2-(2,2-dimethylcyclopropanecarboxamido)-2-heptenoic free acid compound, dependent Claim 20 recites one of four "salt forms" which are "pharmaceutically acceptable salts" as recited in Claim 9. Claim 20 depends from both Claim 19 and Claim 9.

By reciting only heptenoate sodium, potassium, calcium, or magnesium salt compounds, Claim 20 defines a class of compounds that are mutually exclusive from the free acid compound that is defined by Claim 19. In Claim 19, R^1 of independent Claim 9 must be hydrogen, and in Claim 20, R^1 of independent Claim 9 cannot be hydrogen, so the compound must be one of the specifically recited pharmaceutically acceptable salts.

In view of the clear and unambiguous language of dependent Claim 20, Claim 20 should be construed to encompass only the recited heptenoate salt compounds, and not the free heptenoic acid compound. This claim construction issue, which is a pure question of law based on the grammatical structure of the claims, including an independent claim which recites alternative, mutually exclusive groups and a dependent claims which recites only one of the

groups, is governed by *Pfizer, Inc. v. Ranbaxy Labs., Ltd.*, 457 F.3d 1284, 1291 n.6 (Fed. Cir. 2006).

In *Pfizer v. Ranbaxy*, the independent claim at issue, like present Claim 9, recited in the alternative (1) atorvastatin acid; or (2) atorvastatin lactone; or (3) "pharmaceutically acceptable salts thereof." 457 F.3d at 1291. Intermediate dependent Claim 2, like present Claim 19, recited only one of the three alternatives, *i.e.*, "atorvastatin acid." *Id.* Dependent Claim 6, which depended from intermediate Claim 2, like present Claim 20 recited only a specific salt of atorvastatin acid ("the hemicalcium salt of the compound of claim 2"). The independent and dependent claim structure in *Pfizer v. Ranbaxy* was thus substantively identical to the claims at issue in this case: an independent claim recited (1) an acid or (2) pharmaceutically acceptable salts thereof; an intermediate dependent claim was limited to the free acid, and a further dependent claim, which depended from the intermediate claim, was limited to a salt of the compound claimed in the intermediate claim, *i.e.*, a salt of the acid. *Id.*

The Federal Circuit interpreted Claim 2 (drawn to the acid) to exclude pharmaceutically acceptable salts, because this dependent claim did not contain the "pharmaceutically acceptable salts" language which was used in Claim 1. The intrinsic evidence, *i.e.*, the language of the claims at issue, precluded a broader construction of dependent Claim 2. *Pfizer*, 457 F.3d at 1291 and n.6.

The Federal Circuit also interpreted dependent Claim 6 (drawn to the salt of the acid of claim 2) as being limited to the salt form that was expressly recited, *i.e.*, to exclude an acid form of the compound. *Id.*

Under *Pfizer v. Ranbaxy*, in view of the express language of dependent Claims 19 and 20, which claim different, non-overlapping groups that are recited in the alternative in independent

Claim 9, and in view of the specification's unequivocal distinction between the free acid that is claimed in Claim 19, and the pharmaceutically acceptable salts that are claimed in Claim 20, Claim 20 should be construed as being limited to the four pharmaceutically acceptable salts that are specifically recited, and to exclude the free acid that is separately claimed in Claim 19.

The consequence of this construction is clear from *Pfizer v. Ranbaxy*. Properly construed, Claim 20 cannot as a matter of law include any free acid compound recited in Claim 19. Based on the intrinsic evidence, and more particularly the alternative definition of specific R^1 groups in independent Claim 9, which are separately claimed in Claims 19 and 20, it is clear that Claim 20 is invalid under 35 U.S.C. §112, fourth paragraph, because it does not include each limitation of Claim 19 as required by the statute. *Pfizer*, 457 F.3d at 1292. As the Federal Circuit observed in that case, the dependent salt compound claim could have properly been drafted as depending from the independent claim, which included a salt, or could have been drafted as an independent claim. *Id.* Indeed, the court "recognize[d] that the patentee was attempting to claim what might otherwise have been patentable subject matter" agreeing with the district court's finding that the invalid claim was "unambiguous to the extent that the patentee intended to claim the hemicalcium salt of atorvastatin acid." *Id.* at 1292 and n.7. The district court also recognized that "[a]s a matter of standard chemical nomenclature, chemists typically refer to a salt of an acid, even though they are aware that the complete acid is technically no longer present in the salt form." *Id.* at 1292 n.7. None of these circumstances permitted a construction of the atorvastatin acid claim which could encompass a salt of the acid.

The same reasoning governs the construction of Claims 19 and 20 of the present case, and compels the conclusion that Claim 20 is invalid because it does not include each limitation of Claim 19. If the Court adopts Ranbaxy's proposed construction, it should hold Claim 20 to be

invalid under 35 U.S.C. §112, fourth paragraph. As in *Pfizer v. Ranbaxy*, Claim 20 "does not narrow the scope of claim [19]; instead, the two claims deal with non-overlapping subject matter" because of their relationship to the independent claim. 457 F.3d at 1291.

Claim 20 is limited to the four recited heptenoate salt compounds, and to the isomers of each in which the 7-(L-2-amino-2-carboxyethylthio) substituent has the R configuration. However, Claim 20 clearly encompasses both isomeric forms of each of the recited heptenoate salt compounds within the scope of the claim, having a 2-(S)-(2,2-dimethylcyclopropane-carboxamido) group or a 2-(R)-(2,2-dimethylcyclopropanecarboxamido) group. Claim 20 should be construed to include these two forms and mixtures thereof, of each of the four recited heptenoate salt compounds, in order to give Claim 20 its full literal scope.

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Dated: December 11, 2007

UNITED STATES DISTRICT COURT
DISTRICT OF DELAWARE

CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on December 11, 2007, I electronically filed the foregoing document with the Clerk of Court using CM/ECF and caused the same to be served on the defendant at the addresses and in the manner indicated below:

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EXHIBIT A

GLOSSARY OF CHEMICAL TERMS IN SUPPORT OF RANBAXY'S BRIEF ON CLAIM CONSTRUCTION

alkyl	a hydrocarbon substituent (or "radical") containing one or more carbon atoms (and hydrogen atoms), which may have a linear, branched or cyclic structure formed by single-bonded carbon atoms (A2523-2524, A2532-2534 and A2669)
methyl	an alkyl substituent of 1 carbon atom (A2535-2536, A2669, A2672 and A2675)
ethyl	an alkyl substituent of 2 carbon atoms (A2513, A2537, A2669 and A2672)
propyl	an alkyl substituent of 3 carbon atoms, which may be linear, or branched (isopropyl), or cyclic (cyclopropyl) (A2513, A2518, A2538, A2669-2670 and A2672)
butyl	an alkyl substituent of 4 carbon atoms, which may be linear, or branched (isobutyl, tertiary butyl), or cyclic (cyclobutyl) (A2513-2514, A2518, A2530, A2669-2670 and A2672)
pentyl	an alkyl substituent of 5 carbon atoms, which may be linear, or branched, or cyclic (cyclopentyl) (A2513-2514, A2543, A2669-2670 and A2672)
hexyl	an alkyl substituent of 6 carbon atoms, which may be linear, or branched, or cyclic (cyclohexyl) (A2513-2514, A2518, A2544, A2669-2670 and A2672)
heptyl	an alkyl substituent of 7 carbon atoms, which may be linear, or branched, or cyclic (cycloheptyl) (A2513-2514, A2518, A2545, A2669-2670 and A2672)
2-heptenoic acid	an acid having a 7-carbon chain, in which there is a double-bond between the carbons at the 2-position and the 3-position, terminating with a free acid –COOH group (A2513-2518, A2526, A2546, A2554 and A2666-2667)
ester	a derivative of an acid, in which the hydrogen of the free acid is replaced with a substituted or unsubstituted alkyl group to form the group -COO-alkyl (A2517, A2526, A255 and A2563)

EXHIBIT A